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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,698	09/08/2006	Klaus Hellerbrand	DFMP/SCIL 1001 US-PAT	9077

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EXAMINER	
HEYER, DENNIS	

ART UNIT	PAPER NUMBER
1628	

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04/20/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/598,698	HELLERBRAND ET AL.	
	Examiner	Art Unit	
	DENNIS HEYER	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/24/2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 4, 6, 8 – 9, 11 – 17, 48 and 51 – 53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 6, 8 – 9, 11 – 17, 48 and 51 – 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 24, 2011 has been entered.

Acknowledgement is made of Applicant's remarks and amendments filed February 24, 2011. Acknowledgement is made of the amendment to independent method Claim 1 which now includes the limitations "providing a container having a receptacle" and, 'wherein the receptacle of the container is coaxially located within a container housing'.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of Claims

Claims 1, 4, 6, 8 – 9, 11 – 17, 48 and 51 – 53 are currently pending.

Claim rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 6, 8, 11 – 12 and 16 – 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song in WO 2005/016399 A1 (priority date: August 11, 2004, published: February 24, 2005; previously cited in the Office Action mailed August 27, 2010) in view of Talalay in US patent 4,063,367 (published: December 20, 1977; previously cited in the Office Action mailed August 27, 2010) and Graff, D.A. in US Patent 5,316,146 (published: May 31, 1994).

Song teaches a medical device comprising a substrate, a therapeutic agent containing region over the substrate which comprises a therapeutic agent and an antioxidant (a coating) as well as methods of making said coated devices (Abstract).

Song teaches providing a solution comprising a solvent, a therapeutic agent and an antioxidant, contacting the solution with a medical device substrate and then removing the solvent from the solution to form a therapeutic-agent-containing region (Abstract; instant Claim 4). Song teaches 'dipping techniques' (equivalent to inserting the device into the solution) as a preferred solvent-based technique for contacting the device with a solution (p [0042]; instant Claim 1, step (c)).

The teaching of "dipping" to coat a medical device with a therapeutic agent-containing solution is reasonably construed by one of ordinary skill in the art as teaching Claim 1(a) and 1(b) drawn to providing the required receptacle, and the solution within said receptacle in order that the medical device can be dipped (i.e. coated, Claim 1, step (1c)).

Instant Claim 6 is drawn to immobilization of the pharmaceutically active substance to an inorganic or organic bioresorbable material. Song teaches that the process of contacting a substrate containing a previously formed polymer layer with a solution containing a therapeutic agent (pharmaceutically active substance) results in said agent being "imbibed by the polymer" (p [0044]). One of ordinary skill would reasonably construe the process of "imbibing" (defined as: to take in, absorb) to meet the limitation of 'immobilized' as defined in p [0053] of the instant specification. Song

also teaches that the imbibing (immobilization) may occur within a bioresorbable material including polypeptide biopolymers as coatings (p [0039]).

Song teaches the solution contacting the medical device comprises non-active ingredients, specifically, a polystyrene-polyisobutylene block copolymer (page 13, Example 3, paragraph [0050]; instant Claim 8). Song teaches the solution contacting the medical device is an organic solvent, tetrahydrofuran (page 13, Example 3, paragraph [0050]; instant Claim 12). Song teaches the solution contacting the medical device contains an antioxidant, said antioxidant comprising BHT, BHA or tocopherol (Abstract, step a (iii), paragraph [0009], see also, page 13, Example, paragraph [0050]; instant Claim 14). Song teaches that the medical device may be a stent (page 13, Example 3, paragraph [0050]) and that the medical device includes any coated substrate which can comprise, for example, metal (page 3 – 4, paragraph [0020]) (instant Claims 16 and 17).

Claim 1, step (d) recites the limitation that the device is coated by "starting isothermal drying of the device while the device remains held within the solution held within the container, thereby removing the volatile components from the solution of the coating substance".

Song teaches the step of drying a coated medical device in an oven but does not expressly teach the process of isothermal drying as recited in instant Claim 1, step (d).

Song also does not explicitly teach the limitation in amended Claim 1, step (a), which requires that the receptacle into which the medical device is dipped (inserted) is

coaxially located within a container housing or, the method recited in instant Claim 11 "wherein the container becomes a packaging container for the device".

Talalay teaches a method for drying liquid contained in a receptacle comprising a biologically active liquid solid composite comprising the step of passing a stream of dry air over said container in order to evaporate the liquid from said container (Claims 1 and 3). Talalay does not use the term 'isothermal drying', however, Talalay teaches a process in which the temperature is held constant (column 3, lines 56 – 58) and thus the drying process of Talalay is considered to fall within the scope of the process of 'isothermal drying' disclosed on page 20, lines 7 – 25 of the present specification. Talalay teaches the receptacles are subsequently subjected to a vacuum to complete the drying operation (removal of liquid), filled with an inert gas and then sealed (column 2, lines 2 – 7; see also Claims 3 and 4). Talalay teaches that the process of drying the biologically active material and sealing the receptacles ensures a long shelf life (column 2, lines 10 – 13). Talalay teaches that the vacuum step of the process removes residual moisture from the containers as well as oxygen and airborne contaminants.

Thus, Song in combination with Talalay teach a method for coating a device (instant Claim 1) wherein the receptacle becomes the packaging container. The combination of references do not explicitly teach the limitation of amended Claim 1 which requires that the *receptacle is located coaxially within a container housing*. The combination of references therefore does not teach a container which becomes the packaging container for the device (instant Claim 11) because the packaging container now requires the receptacle to be located coaxially within a container housing.

Graff teaches a transport container (i.e. a packaging container, instant Claim 11) for transporting fragile articles such as test tubes or vials in order to protect the contents from impact shocks associated with transport and thus prevent breakage of the vials. (Abstract). Figure 3 (below) of Graff illustrates the coaxial orientation of the vial (a receptacle, element '60') within the container housing (transporter base, element 14').

FIG. 2

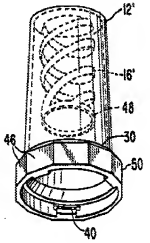
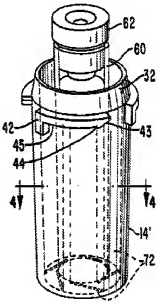


FIG. 3



For further clarity, it is noted that the housing also includes a cap (FIG. 2, element 12') which is placed on top of the base in order to completely encapsulate the vial receptacle contained within the housing.

Graff teaches that the vial transporter (a housing) prevents or minimizes leakage from a vial (a receptacle) during transport and that even if fluid were to leak from the receptacle it would be contained within the transport container (the housing) (column 2, lines 56 – 66). Graff teaches the transporter (a housing) restrains the vial (the

receptacle) from moving in the radial and longitudinal directions and away from the walls of the transporter (housing). Thus the housing walls are better able to absorb shocks or impact associated with transport and prevent damage to the receptacle (columns 2 – 3, bridging paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made, to modify the drying method for the coated medical device of Song using the isothermal drying process taught by Talalay. One would have been motivated to do so because Talalay teaches the method allows one to seal the receptacle (container) following removal of moisture (liquid) and thus ensure a longer shelf life.

Further, one would have been motivated to remove volatile components from the coated medical device of Song by carrying out the isothermal drying method taught by Talalay because Song teaches that it may be beneficial to maintain a therapeutic agent coated onto a medical device in a non-oxidizing environment during the course of its formation (page 12, p [0046] and [0047]) and, that subsequent to it's formation, it may be beneficial to place the coated medical device into packaging (a receptacle) that has been evacuated or into which an inert gas has been introduced in order to maintain a non-oxidizing environment (p [0047]).

It would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made, to modify the receptacle in the method of Song in combination with Talalay for coating a medical device with a housing in which the receptacle is located coaxially within said housing. One would have been motivated to

do so because Graff teaches that vials (receptacles) contained coaxially within a housing have a reduced risk of breaking and releasing the fluid contained within during transport because the housing walls can absorb shocks during transport. Accordingly, one would have been motivated to prepare the coated medical device in a receptacle maintained in an inert gas or non-oxidizing environment (Song) to extend it's shelf life (Talalay) in a packaging container housing wherein the receptacle is located coaxially (Graf), in order to minimize, upon transport of the receptacle, damaging or breaking the receptacle and undesired release of the inert gas (a fluid) contained therein.

Claims 9, 13, 48 and 52 – 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song in WO 2005/016399 A1 (priority date: August 11, 2004, published: February 24, 2005) in view of Talalay in US patent 4,063,367 (published: December 20, 1977) and Graff, D.A. in US Patent 5,316,146 (published: May 31, 1994), as applied to Claims 1, 4, 6, 8, 11 – 12 and 16 – 17, and further in view of Kohnert *et al.* in WO 2003/043673 (published: May 30, 2003; previously cited in the Office Action mailed November 27, 2009).

As noted in the 103(a) rejection above, the combination of Song, Talalay and Graff renders obvious the method of coating a device recited in instant Claims 1, 4, 6, 8, 11 – 12 and 16 – 17.

The combination of references do not teach a coating substance comprising calcium phosphates (instant Claim 9), or the device being calcium phosphate or β-tricalcium phosphate (instant Claims 52 – 53). The references also do not teach an acidic aqueous contacting solution (instant Claim 13), or that the method of instant

Claim 1 provides a homogeneous distribution of the coating on the device (instant Claim 48).

Kohnert teaches devices having osteoconductive and osteoinductive properties (Title) comprising a carrier containing calcium phosphate wherein said carrier is homogeneously coated with protein (Abstract). Kohnert teaches a method for preparing said devices comprising providing a solution comprising an osteoinductive protein and a buffer and contacting the solution with a carrier containing calcium phosphate.

Kohnert teaches that the contacting solution comprises a carrier containing calcium phosphate (page 6, 3rd paragraph; instant Claim 9). Kohnert teaches that the device may be made of calcium phosphate or β-tricalcium phosphate (Claim 11, instant Claims 52 and 53). Kohnert teaches that the contacting solution comprises a buffer, and that, preferably, the preferred pH is between 4 and 6 (page 8, paragraphs 3 and 4), which meets the limitation of the instant Claim that the contacting solution be an aqueous acidic solution (instant Claim 13).

Instant Claim 48 is drawn to a homogeneous distribution of the coating on the device. Kohnert teaches a method that provides a homogeneous coating on the surface of the device (page 6, paragraph 3 to page 7, paragraph 1, in particular step (c)) and teaches that an advantage of the present invention is the homogeneous coating which is achieved during the coating process (page 7, paragraph 4).

One would have been motivated to modify the method of coating the device of Song, Talalay and Graf, when the solution is an acid aqueous solution (preferably pH 4 – 6) because Kohnert teaches that said pH ranges prevent the precipitation of the bone

morphogenic member protein (BMP) family member, GDF-5, from solution and insures the device achieves a homogeneous coating (page 7, paragraph 3 and 4) as nonhomogeneous coatings can lead to decreased osteoinductive properties (page 6, 2nd paragraph). Therefore, Kohnert provides specific motivation to optimize the nature of the coating solution (from an organic solvent to an aqueous acidic solution at pH 4 – 6) of Song by teaching that the protein-derived therapeutic agents taught by Song, which include BMP protein (Song, p [0033]), will remain dissolved in aqueous solution at pH 4 – 6.

One would have been motivated to modify the method of coating a medical device rendered obvious by the combination of Song, Talalay and Graff with a bioresorbable material such as calcium phosphate and β-tricalcium phosphate because Kohnert teaches that said materials are effective bone-replacement materials (page 1, paragraph 2) and thus are art-recognized as components of medical devices.

Claim 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song in WO 2005/016399 A1 (priority date: August 11, 2004, published: February 24, 2005) in view of Talalay in US patent 4,063,367 (published: December 20, 1977) and Graff, D.A. in US Patent 5,316,146 (published: May 31, 1994), as applied to Claims 1 – 5 and 8, 11 – 12, 14 and 16 – 17 above, and further in view of Lee *et al.* in US patent 5,571,523; published November 5, 1996; previously cited in the Office Action mailed November 27, 2009).

As noted in the 103(a) rejection above, Song in combination with Talalay and Graff renders obvious the method of instant Claim 1. The references render obvious

that the solution contacting the medical device comprises an antioxidant (such as BHT, BHA or tocopherol, instant Claim 14), but does not expressly teach methionine as the antioxidant.

Lee teaches a method for inhibiting artherosclerosis by contacting an artery with an apoptosis-inducing amount of an antioxidant (Abstract) in which methionine is a preferred antioxidant (column 1, lines 37 – 43, Claim 7). Lee teaches that one means for locally delivering the antioxidant is by providing (coating) the antioxidant on the surface of a vascular catheter (a medical device) which contact the wall of a blood vessel (column 1, lines 64 – 67).

Thus, it would have been *prima facie* obvious to one skilled in the art, at the time the invention was made, to modify the method rendered obvious over Song, Talalay and Graff and use methionine as an antioxidant in place of tocopherol, BHA or BHT on a coated medical device, such as a stent or catheter. One would have been motivated to do so because methionine is effective at inhibiting arteriosclerosis and has been taught by Lee that a means of delivering methionine to a blood vessel is *via* an implantable medical device.

Claim 51 is rejected under 35 U.S.C. 103(a) as being unpatentable over Song in WO 2005/016399 A1 (filing date: August 11, 2004, published: February 24, 2005) and Talalay in US patent 4,063,367 (published: December 20, 1977), as applied to Claims 1 – 5 and 8, 11 – 12, 14 and 16 – 17 above, and further in view of Gao *et al.* in US patent 6,113,993 (published: September 5, 2000; previously cited in the Office Action mailed November 27, 2009).

As noted in the 103(a) rejection above, Song in combination with Talalay and Graff render obvious the method of instant Claim 1. Song in combination with Talalay and Graff render obvious a method for coating implantable medical devices in which the coated substrate comprises metal (paragraph [0020]) but do not expressly teach a device made of titanium or a titanium alloy as recited in instant Claim 51.

Gao teaches a method of coating an implant with a calcium phosphate compound on a titanium substrate (Abstract). Gao teaches that orthopaedic implants are commonly made of titanium alloy because of its corrosion resistance to body fluids. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made, to adapt the method of coating a medical device made of metal, rendered obvious over Song, Talalay and Graff, to a device made of titanium. One would have been motivated to do so because implants are commonly made of titanium alloys to gain the benefit of their corrosion resistance to body fluids.

Response to Arguments

Applicant's arguments filed February 24, 2011 with respect to the rejections under 35 U.S.C 103(a) in light of the amendments to Claim 1 have been fully considered but are moot in view of the new ground(s) of rejection.

Conclusion

Claims 1, 4, 6, 8 – 9, 11 – 17, 48 and 51 – 53 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DENNIS HEYER whose telephone number is (571)270-7677. The examiner can normally be reached on Monday-Thursday 8AM-5PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, BRANDON FETTEROLF can be reached at (571)272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/DENNIS HEYER/
Examiner, Art Unit 1628

/Timothy P Thomas/
Primary Examiner, Art Unit 1628